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AGGLUTINATION IN INFLUENZA

KIRSTEN UTHEIM

From the Department of Pediatrics, Washington University, and the St. Louis Children's Hospital, St. Louis

During the last epidemic in St. Louis in February, 1920, agglutination tests were made on serum from patients with influenza in the St. Louis Children's Hospital and the Barnes Hospital in order to determine (1) whether the serum of the patient agglutinates the influenza bacillus obtained from the same patient, (2) whether agglutination takes place with heterologous strains.

Studies of the agglutination reaction in influenza have not given uniform results. The first attempt to find specific antibodies in influenza serum was made in 1903 by Cantani[1] who examined three patients, two with acute influenza pneumonia, and their serum failed to cause agglutination; the serum of the third patient with uncomplicated influenza caused agglutination at 1:200. No further study was made until 1916, when Levinthal[2] found a strongly positive agglutination in 6 cases of uncomplicated influenza of which 3 were positive in a dilution of 1:400, 2 in 1:200 and 1 in 1:100. A seventh patient had a complicating pneumonia and caused agglutination 1:200. Levinthal emphasizes the diagnostic value of this test. I shall mention a few only of the studies that have been made recently.

Flemming[3] obtained positive agglutination in all of 21 cases but in low dilution, once at 1:1,000, twice at 1:128, three times at 1:64, in ten at 1:32, in four at 1:16, and in one at 1:8. Most of the patients were convalescent from 7 to 10 days after the onset of influenza. His control tests were all negative.

Duval and Harris[4] found agglutination in most instances, but not in a dilution above 1:80 and often as early as the third day of the disease. Normal blood reacted in a few instances but never above 1:20.

Martha Wollstein[5] examined serum from 11 patients during the second week of illness; 5 mild cases of bronchopneumonia gave positive results in a dilution of 1:100. Of 6 patients with uncomplicated influenza, 4 gave negative results and two positive, in dilutions of 1:40. The control serums sometimes gave a positive reaction in dilutions of 1:10. The tendency to spontaneous clumping, which was the chief difficulty, suggests that agglutination reactions with bacillus of Pfeiffer may not be satisfactory. Wollstein, like most of the authors who have worked with vaccinated patients, found that agglutinins are developed in the blood from 6 to 10 days after inoculation.

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[1] Ztschr. f. Hyg. u. Infectionskrankh., 1903, 42, p. 505.

[2] Ztschr. f. Hyg. u. Infectionskrankh., 1918, 86, p. 1.

[3] Lancet, 1919, 1, p. 138.

[4] Jour. of Infect. Dis., 1919, 25, p. 384.

[5] Jour. Exper. Med., 1919, 30, p. 555.

From this short résumé it can be seen that all the authors mentioned found agglutinins for influenza bacilli in the blood of patients with influenza, present in greater or less strength and in accordance with the frequency of positive results more or less stress has been placed on the diagnostic and etiologic value of the test.

No studies on agglutination of homologous and heterologous strains by the serum of patients appear to have been made. Park[6] and his co-workers came to the conclusion that while specific agglutination with the homologous serum was obtained with the serum of immunized rabbits, each strain seemed to be individual in its immunologic action.

Small and Dickson[7] recently found characteristic agglutination with some strains so that influenza bacilli might be separated into four groups.

Passing to my own observations, it must first be mentioned that the antigen was prepared in the following way: 48 hour cultures grown on blood agar and originally obtained from the nose or throat by Dr. H. H. Bell and Dr. White were suspended in 0.8% salt solution. After thoroughly shaking, a homogeneous emulsion was usually obtained which did not show any evidence of self agglutination. Only in one instance was it necessary to discard the results on account of spontaneous clumping.

After 4 hours' incubation at 37 C. the tubes were put in the icebox and the result read 24 hours after mixtures were made.

Thirty strains were isolated from 30 patients during the first days after admission to the hospital and tested with serum from these patients during different stages of the disease. Of these, 11 (36%) gave a positive agglutination with their own bacilli, 6 in a dilution of 1:160; 4 in 1:80 and 1 in 1:20.

These serums were then tested with heterologous strains. With the exception of one strain, which gave an agglutination of 1:40 with three serums of other patients, there was found no cross agglutination in any serum tested. Each strain seemed to be individual in its immunologic reaction.

Five control serums from persons who gave no history of having had influenza were tried with different strains. In one instance an agglutination at 1:20 was obtained. In all other instances the result was negative.

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[6] Jour. Am. Med. Assn., 1919, 73, p. 318.

[7] Jour. Infect. Dis., 1920, 26, p. 230.

The blood of 9 patients was examined during different stages of the disease; 8 showed a constantly negative result while in one instance the agglutination became positive in a dilution of 1:80 in the convalescent stage of the disease. Two strains were isolated from this patient and both gave the same result on agglutination.

RESULTS OF TESTS

No.	Day of Disease	Agglutination	Age	Remarks
1	6	1:160	41 years	Bronchopneumonia
2	11	1:160	35 years	Convalescent after uncomplicated influenza
3	11	1:80	38 years	Convalescent after uncomplicated influenza
4	11	1:80	25 years	Convalescent after uncomplicated influenza
5	10	1:160	68 years	Convalescent after uncomplicated influenza
6	8	1:160	5 years	Convalescent after uncomplicated influenza
7	1	1:80	8 years	Convalescent after uncomplicated influenza
8	14	1:160	10 years	Influenza with lobar pneumonia; fever during 13 days
9	7	1:160	2 years	Influenza with slight bronchitis
10	15	0	1 year	First afebrile day after light lobar pneumonia. Discharged on 19th day, recovered
	19	1:80	1 year	
11	8	1:20	13 months	Influenza with bronchopneumonia which disappeared 16 days after onset
	11	0	13 months	
	25	0	13 months	
12	13	0	27 years	Uncomplicated influenza
13	12	0	23 years	Convalescent after uncomplicated influenza
14	7	0	18 years	Uncomplicated influenza
15	10	0	30 years	Influenza with bronchopneumonia; fever during first 12 days
16	10	0	32 years	Convalescent after uncomplicated influenza
17	8	0	3 years	Influenza with fever during whole time in hospital
	11	0	3 years	
18	16	0	14 years	Influenza with bronchopneumonia. Fever during 31 days
	30	0	14 years	
19	9	0	2 years	Influenza with fever 10 days
20	13	0	4 years	Influenza with bronchopneumonia; delayed resolution; fever in hospital
	27	0	4 years	
21	7	0	13 months	Influenza with bronchopneumonia and otitis media; fever 10 days
22	8	0	2 years	Influenza with bronchitis; fever 12 days
23	10	0	6 years	Influenza with chronic bronchopneumonia. Tuberculosis
	13	0	6 years	
24	8	0	7 years	Influenza with otitis media
25	7	0	6 years	Influenza with chronic bronchopneumonia
	10	0	6 years	
	24	0	6 years	
26	4	0	11 years	Bronchopneumonia in both lungs
	29	0	11 years	
27	5	0	4 years	Uncomplicated influenza
	9	0	4 years	
28	7	0	1½ years	Influenza with bronchopneumonia; fever during 7 days
29	13	0	5 years	Influenza with bronchopneumonia; lungs not clear at discharge from hospital
30	10	0	3 years	Influenza with bronchopneumonia

It is of interest that 3 strains of the influenza bacillus were isolated from the same plate made from the throat of patient 10. These strains were shown by Dr. Bell to be distinctly different by agglutination and absorption tests with monovalent immune serum. Only one of these strains gave agglutination with the patient's serum. The strains isolated from Case 10 are represented by Nos. 25, 26, and 27, on Chart 1 of Dr. Bell's report [8] No. 25 gave agglutination.

During uncomplicated influenza the body does not always form antibodies against the influenza bacillus. It would have been desirable to have observed these patients after complete recovery, but after discharge from the hospital it was not possible to make the further examinations.

SUMMARY

Of 30 strains isolated from patients with influenza 11, or 36 per cent., gave agglutination with the patient's serum. Seven of these occurred in uncomplicated influenza, and 4 in influenza pneumonia. Of the remaining 19 negative cases, 10 had pneumonia.

Of 30 strains only one was agglutinated by heterologous serum.

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[8] Jour. Infect. Dis., this issue.